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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/698,855	10/31/2003	Jens Holm	04305/100M237-US1	9333

7278 7590 06/27/2007

DARBY & DARBY P.C.
P.O. BOX 770
Church Street Station
New York, NY 10008-0770

EXAMINER	
TSAY, MARSHA M	
ART UNIT	**PAPER NUMBER**
1656	

MAIL DATE	DELIVERY MODE
06/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/698,855	HOLM ET AL.	
	Examiner	Art Unit	
	Marsha M. Tsay	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26,27 and 29-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26,27 and 29* is/are rejected.

7)☒ Claim(s) *30-32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

This Office action is in response to Applicants' remarks received April 20, 2007. Claims 1-25, 28, 33-92 are canceled. Claims 26-27, 29-32 are pending currently under examination.

Applicants' arguments have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous Office actions are hereby withdrawn.

Priority: The priority date is November 1, 2002.

Objections and Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-27, 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a modified Dau c 1 scaffold protein depicted as SEQ ID NO: 4 and comprising at least two primary mutations selected from the group recited in claims 30-32, does not reasonably provide enablement for variants of a scaffold protein Dau c 1 having a three-dimensional folding pattern that is structurally similar to that of the naturally occurring allergen, said protein variant comprises two or more primary mutations spaced by at least one non-mutated amino acid residue, each primary mutation introducing into the scaffold protein at least one amino acid residue identical or homologous to the amino acid residue or residues in corresponding position in the naturally occurring allergen. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claim reads on a recombinant protein variant wherein the protein variant is a variant of a scaffold protein (Dau c 1), wherein the scaffold protein has a three-dimensional folding pattern that is structurally similar to the naturally-occurring allergen (Bet v 1).

Applicant has claimed a genus of modified Dau c 1 allergen proteins and has provided examples of modifications to SEQ ID NO: 4 to support this genus. The specification provides support for the modification of Dau c 1 scaffold (SEQ ID NO: 4) (Example 2 and Fig. 17). However, the results do not provide support for the entire claimed genus of modified allergens.

First, while claim 29 recites that the modified scaffold protein Dau c 1 comprises two or more primary mutations spaced by at least one non-mutated amino acid residue, each primary mutation introduced into the scaffold protein is at least one amino acid residue that is identical or homologous to the amino acid residue or residues in corresponding position in the naturally occurring allergen, it does not specify the reference sequence or along which positions on the sequence that mutations should take place. It is known in the art that amino acid sequence identity of 50% does not guarantee structural similarity (Yuan et al. 1998 Proteins 30: 136-143; previously cited) and that even a single point mutation in a polypeptide sequence can lead to surprising alterations in protein structure and activity (Sergel et al. 2000 J. Virol. 74: 5101-5107; previously cited). As such, it is unclear where mutations need to be made such that the epitope(s) bound by IgE antibodies are affected. Even when a precise amino acid within in the epitope to be altered is identified, the choice of what that amino acid should be mutated to is not predictable since some substituted amino acids reduce IgE binding while others have no effect or

unexpectedly increase IgE binding (Nishiyama et al., US Patent 6187311 and Reese et al., J Immunol, 2005, 175:8354-8364, see entire document, particularly the paragraph that spans pages 8357 and 8358, Table I and Figure 2).

Further, Applicants have also claimed that the instant protein variants (claims 26-27) and the modified Dau c 1 scaffold protein (claim 29) have the ability to induce a protective immune response to a naturally occurring allergen (Bet v 1). Immunotherapy is a well known art technique wherein an allergic patient is given increasing doses of an allergen in an effort to redirect the patient's immune response from a Th2 to a Th1 cytokine profile such that production of allergen-specific IgE is diminished (Blumenthal et al. in Allergens and Immunotherapy, third edition, 2004, pages 37-50, see entire document, particularly pages 43 and 44; previously cited). It is also well known in the art that immunotherapy is not an effective treatment for all individuals, and that in individuals for whom treatment is effective, symptoms of allergic disease are still present, albeit at a diminished level (Niu et al., Respiratory Medicine, Epub on January 3, 2006, see entire document, particularly the bottom of the left column of page 4, the discussion section beginning on page 6 and Figures 1-4 and Tables 2 and 3). On page 43, the specification discloses that raising a protective immune response means to alter the reaction of the immune system towards a naturally occurring allergen in order to avoid the adverse effects associated with allergy. Further, the protective immune response is thought to be mediated largely by generation of a large number of IgG antibodies that presumably block the interaction between allergen and IgE antibodies. A protective immune response most likely also involves stimulation of T-cells. The specification does not appear to have a clear definition as to what constitutes a "protective" immune response based on the language that a protective immune response is

"thought" to be mediated...and that it "most likely" also involves T-cell stimulation. While it is clear that one of ordinary skill can ascertain that the instant protein variants are capable of inducing an immune response, it is uncertain if the immune response can be described as "protective."

Therefore, based upon the breadth of the claimed invention, the difficulty in ascertaining the precise location wherein substitution mutations are to be made, the art recognized problem concerning the unpredictability of which amino acid residues when used for making substitution mutations result in altered IgE binding, and the data from the art and applicant's specification, a skilled artisan would be unable to make and use the full breadth of applicant's claimed invention without conducting an undue amount of research.

Claims 30-32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marsha M. Tsay whose telephone number is 571-272-2938. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Karen Cochrane Carlson

June 20, 2007

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER